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Camitta B M, Thomas E D, Nathan D G, Santos G, Gordon-Smith E C, Gale R P, Rappeport J M & Storb R. Severe aplastic anemia: a prospective study of the effect of early marrow transplantation on acute mortality. *Blood* 48:63-70, 1976.
[Midwest Children's Cancer Ctr., Dept. Pediatrics, Medical Coll. Wisconsin, Milwaukee, WI]

This study compared early bone marrow transplantation with conventional androgen therapy for patients with severe aplastic anemia. Early transplantation more effectively restored normal bone marrow function and descreased the acute mortality of severe marrow aplasia. [The *SCI*® indicates that this paper has been cited in over 155 publications.]

Bruce M. Camitta
Midwest Children's Cancer Center
Department of Pediatrics
Medical College of Wisconsin
Milwaukee, WI 53233

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In 1973, as a hematology fellow with David Nathan, I attended a session of the Polycythemia Vera Study Group devoted to aplastic anemia. Many speakers suggested studying the comparative efficacy of different androgens. I asked Dr. Nathan to suggest that the most important issue was not a comparison of androgens but rather whether or not androgens were effective. A distinguished gentleman on my other side thereupon suggested that if I was convinced of this I should write such a study myself. Before I could respond, "Who are you?", Dr. Nathan introduced me to Dr. E. Donnall Thomas.

The randomized study that emerged was to compare the efficacy of treatment with supportive care (antibiotics, transfusions) alone versus supportive care plus either oral or intramuscular androgen. Because the Seattle team had encouraging results with bone marrow transplantation,[1,2] patients who had a histocompatible sibling donor could receive a marrow transplant or be randomized as above.

Since bone marrow transplantation would destroy a patient's residual "normal" bone marrow, we wanted to limit our study to aplastic anemia patients who had more severe disease. However, review of previous reports suggested a multiplicity of possible prognostic criteria. I decided that any definition of severe aplastic anemia should be simple and reproducible. Peripheral blood criteria were chosen below which patients would have an increased risk of fatal bleeding or infection. The criterion for decreased red-cell production was a reticulocyte count corrected for the hematocrit rather than the uncorrected count as in previous studies. Bone marrow criteria were included primarily to rule out underlying diseases.

Early in the study, it became apparent that, compared to nontransplant regimens, early bone marrow transplantation more effectively restored normal marrow function and decreased the acute mortality of severe aplastic anemia. The short-term survival advantage persisted with longer follow-up.[3] We also noted that androgen therapy did not improve prognosis in nontransplanted patients with severe aplastic anemia.

I believe that this paper has been cited frequently for several reasons. First, the demonstration that bone marrow transplantation was superior to standard medical therapy stimulated an enormous expansion of interest both in bone marrow transplantation (a new therapeutic tool) and in aplastic anemia (now a treatable disease). Second, the criteria for severe disease defined a group of patients with high mortality (75-80 percent) despite conventional medical care. These patients are prime candidates for bone marrow transplantation or for investigations of other innovative therapies. In addition, use of standard criteria for disease severity has enabled more meaningful comparison of laboratory and therapeutic studies at different institutions. Finally, the suggestion, subsequently confirmed,[3] that androgens are not effective therapy for severe aplastic anemia removed an enormous impediment to investigation of new therapies. Use of bone marrow transplantation or antilymphocyte globulin as *initial* treatment of severe aplastic anemia now results in 50 to 90 percent long-term survival[4] in comparison to only 20 percent survival at the time the study reported in this paper was begun.

1. **Thomas E D, Buckner C D, Storb R, Neiman P E, Fefer A, Clift R A, Slichter S J, Funk D D, Bryant J I & Lerner K E.** Aplastic anaemia treated by marrow transplantation. *Lancet* 1:284-9. 1972. (Cited 150 times.)
2. **Storb R, Thomas E D, Buckner C D, Clift R A, Johnson F L, Fefer A, Glucksberg H, Giblett E R, Lerner K G & Neiman P.** Allogeneic marrow grafting for treatment of aplastic anemia. *Blood* 43:157-80, 1974. (Cited 270 times.)
3. **Camitta B M, Thomas E D, Nathan D G, Gale R P, Kopecky K J, Rappeport J M, Santos G, Gordon-Smith E C & Storb R.** A prospective study of androgens and bone marrow transplantation for treatment of severe aplastic anemia. *Blood* 53:504-14, 1979. (Cited 140 times.)
4. **Camitta B M, Storb R & Thomas E D.** Aplastic anemia: pathogenesis, diagnosis, treatment, and prognosis. Parts 1 & 2. *N. Engl. J. Med.* 306:645-52; 712-18, 1982. (Cited 65 and 35 times, respectively.)

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